

## REMARKS

The Office concluded that the Declaration of Dr. Therese-Marie Jourdier is insufficient to overcome the rejection set forth in the previous Office Action. Thus, claims 10-15 remain rejected under 35 U.S.C. § 103(a) as obvious over Carrano *et al.*, Groswasser *et al.*, Stites *et al.*, and Bouvet *et al.* For the following reasons, the applicants respectfully traverse.

### **The Applicants and the Examiner Have Established the Unexpected Nature of the Results**

The Examiner found the declaration of Dr. Jourdier unpersuasive because “it does not state that the date [sic, data] presented on page 19 does not have a control group.” (Point 5, page 3.) Thus, the Examiner concluded that the declaration was insufficient to establish that the “claimed subject matter solved a problem that was long standing in the art and it is an unexpected result.” (*Id.*)

Objective evidence presented to traverse a rejection under 35 U.S.C. § 103, such as unexpected results, commercial success, long-felt but unsolved needs, failure of others, copying by others, skepticism of experts, etc, must be considered by the examiner. M.P.E.P. § 716.01(a). However, it is the applicant that has the opportunity to implicate any of these secondary considerations in the obviousness analysis as it is the applicant who has the burden of proffering the evidence related to the secondary considerations. *Id.* In this case, the applicant has only raised the issue of unexpected results. Thus, as to the Examiner’s assertion that the declaration is insufficient to establish evidence of a long-felt but unsolved problem (Point 3, page 5; Point 8, page 4), the applicants respectfully submit that such a showing is unnecessary as this secondary consideration was raised for the first time by the Examiner, not the applicants. Furthermore, while solving a long-felt but unsolved need is evidence of non-obviousness, such a showing is not a prerequisite (and, indeed, is only infrequently relied upon); other indicia generally establish non-obviousness.

As to the Examiner’s assertion in Point 5 (page 3) that the applicants’ argument and declaration are insufficient to establish evidence of unexpected results, the applicants respectfully disagree. The Examiner expands upon this in Point 7 of the Office Action by stating “[a]s there are no unexpected results have been provided, such as the thigh quadriceps injection of an antigen is able to get a significant higher local antibody response compared with the antibody induced by injecting same amount of said antigen in other muscles of the body.” Although the application asserts that the

unexpected result is the more general observation that an injection at a site distant from the mucous membrane could bring about a targeted local response (see p. 2 of application), the claims are limited to the thigh as the site distant from the mucous membrane. The Examiner conceded that the results presented on page 19 of the application were unexpected, as evidenced by the Interview Summary mailed October 2, 2003. The applicants similarly noted that the Examiner acknowledged the unexpected nature of the results of presented on page 19 in the Applicant's Statement of Substance of Substance of September 29, 2003, Examiner's Interview mailed October 29, 2003 and in Point 5 of the declaration (page 2). Thus, the file history and objective evidence establish that the results of the instant invention are unexpected.

Furthermore, one of the references relied upon by the Examiner for the obviousness rejection further establishes the unexpected results of the instant invention. The Examiner has pointed out that Bouvet *et al.* teach that a systemic vaccination can be efficient at the genital level and conclude that the possibility of protecting against sexually transmitted diseases by current procedures before the development of true secretory vaccines seems to be of major interest. (See p. 3960.) Bouvet *et al.* suggest that use of current methods of vaccination (*i.e.*, parenteral) could be used for the prevention of sexually transmitted pathogens, as a substitute for local immunization, when local immunization is unavailable, or to complement local immunization. (See p. 3959.) However, Bouvet *et al.* were unable to generate a local immune response (as evidenced by secretory IgA production) via a parenteral injection. (*Id.*) Thus, even if one of skill in the art was motivated by the teaching of Bouvet *et al.* to use the parenteral immunization strategy taught by Groswasser *et al.* and Stites *et al.* for immunizing a human with the vaccine compositions disclosed by Carrano *et al.* to protect against sexually transmitted diseases such as HIV, HPV, HSV and others, it would not be expected that such a method would produce the local immune response recited by the claims. Therefore, the prior art cited by the Examiner also establishes that the results of the instant invention are unexpected.

Because applicants have established that the immune response in the iliac and inguinal lymph nodes following inoculation in the thigh is unexpected, claims to the broader target of the rectogenitourinary mucous membranes and the lymph nodes which drain it are nonobvious. Evidence establishing unexpected results for a species can be used to establish the nonobviousness of a genus if one of ordinary skill in the art would be able to reasonably extend the results to the broader genus.

M.P.E.P. § 716.02 (d). In this case, the declaration establishes that the local immune response in the internal and external iliac lymph nodes and the inguinal lymph nodes following inoculation in the thigh was unexpected. (Point 5). Furthermore, the declaration establishes that the rectogenitourinary lymph node system and mucous membrane is highly complex and integrated, yet one of ordinary skill in the art would understand that an immune response similar to that observed in the internal and external iliac lymph nodes and the inguinal lymph nodes would be present in other lymph nodes of the rectogenitourinary system. (Point 9). Thus, the declaration itself establishes that one of ordinary skill in the art would be able to reasonably extend the results to the broader genus of the rectogenitourinary mucous membranes and the lymph nodes which drain it.

**The Examiner Has Failed to Properly Set Forth the Rejection under 35 U.S.C. § 103**

The M.P.E.P. § 2142 provides the criteria for establishing a *prima facie* case of obviousness: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art references must teach or suggest all the claim limitations. Furthermore, the teaching or suggestion to make the claimed combination must be found in the prior art, and not based on the applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

In addition, when applying 35 U.S.C. § 103, the following tenets of patent law must be followed:

- (A) The claimed invention must be considered as a whole;
- (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;
- (C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and
- (D) Reasonable expectation of success is the standard with which obviousness is determined.

M.P.E.P. § 2141. The applicants respectfully submit that the Examiner has failed to properly follow Office policy in making its rejection under 35 U.S.C. § 103.

The Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness because the teachings of the prior art do not provide a sufficient basis for a reasonable expectation of success of achieving the claimed invention. Bouvet *et al.* teach that “[s]ystemic-derived immunity in human genital secretions reinforces the potential interest in vaccines given by the parenteral route in prevention of sexually transmitted diseases.” (Page 3960). However, this reference only teaches that parenteral vaccinations can induce a systemic-derived antibody response; the parenteral injection was ineffective at producing a local immune response. The authors are explicit on this point: “A significant involvement of the local immune system at the early phase of boosting (day 10), as well as at the late phase of the previous vaccination (day 0), seems to be unlikely, since the level of SIg antitoxins was low enough in genital secretions to be explained solely by the active transport of serum-derived polymers across epithelial cells ...” (page 3960, right column). Thus, nothing in this reference provides a basis for a reasonable expectation of success of achieving a local immune response targeting the rectogenitourinary mucous membrane and the lymph nodes which drain it. This deficiency in the *prima facie* case is not cured by any of the other cited references.

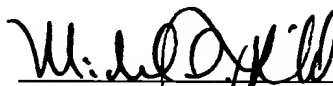
Furthermore, as previously discussed by the applicants, the combination of the cited references does not teach or suggest all of the claim limitations. (See the Office Action responses of May 9, 2003 and September 5, 2003). None of the references, alone or in combination, teaches or suggests both a systemic and a local immune response as specified, as well as targeting the rectogenitourinary mucous membrane and the lymph nodes which drain it.

In summary, the Examiner’s characterization of the both the results and the prior art, and the declaration submitted are sufficient to establish that the results of the invention as claimed are unexpected. Furthermore, a *prima facie* case of obviousness has not been established. In view of the foregoing, the applicants respectfully submit that the present claims cannot be obvious.

If there are any questions or comments regarding this Response or application, the Examiner is encouraged to contact the undersigned attorney as indicated below.

Respectfully submitted,

Date: June 23, 2004



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